Investigation of anti-tuberculosis drugs susceptibility in hospitals of AL-Muthana province*

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Abstract

Anti-tuberculosis drugs susceptibility were conducted among the new case, the findings showed that 18 isolates were resisted to five first drugs treatment (Isoniazid, Rifampicin, Ethambutol, Streptomycin and Pyrazinamide) among 131 isolates with different resistance patterns that monoresistance was shown in 12 (9.2%), 2 drugs resistance in 3 (2.3 %), 3 drugs in 2 (1.5 %) and 4 drugs in 1(0.76) patients. The MDR was found in 6 (4.6 %) patients. *This work is part from PhD thesis

Introduction

Tuberculosis is one of the commonest infectious diseases in the world today, with over 8 million new cases and 2 million deaths occurring annually (WHO, 2009). Although drug resistance was observed even in the early days of chemotherapy nearly 50 years ago, the current threat is due to the emergence of strains resistant to the two most potent anti-tuberculosis drugs i.e., Isoniazid (INH) and Rifampicin (RIF) (Venkataraman and Paramasivan, 2003). The resistance of MDR-TB was

found in Dohuk, Kurdistan (Merzaa *et al*., 2011). Patients infected with MDR-TB strains not only pose a threat to themselves but to the community as well. Therefore, the report was aimed to detect drug resistant strains at the earliest so that appropriate therapy can be initiated which will reduce the morbidity and mortality in infected patients and also prevent the spread of multi-drug resistant strains in the community.

Methods

The work was carried out in the Department of biology/Science College/Al-Muthana University and chest hospital/ Al-Muthana province. One hundred thirty one clinical isolates of *M. tuberculosis* from new cases of patients identified using morphological and biochemical properties as per standard protocol (Kantor *et al*., 1998) were selected from 2010 to 2011. All isolates were stored at -70ºC and sub cultured to obtain a fresh culture before use. .

Drug susceptibility testing

1% proportion plate susceptibility assays by previously described methods (Canetti *at el*, 1969). The Lowenstein-Jensen (LJ) medium in screw-capped tubes (28 ml) was used with and without incorporation of drugs at the recommended concentrations. The drug concentrations used were Isoniazid 0.2 µg/ml, Rifampicin 40 µg/ml, Ethambutol (2.0 µg/ml, Streptomycin 4.0 µg/ml and Pyrazinamide 100 µg/ml (critical concentration).

Reading of the results

Resistance was expressed as the percentage of colonies on drug-containing media in comparison to the growth on drug free medium at the critical concentrations of the substances. The reading was taken on

the 28th day and if a strain was susceptible it was further incubated and a second reading taken on the 42nd day as the final reading (Canetti *at el*, 1969). Sigma plot software (version 11) was used to calculate (*p-value*) of different in characteristics of tuberculosis patients as well as the different in the drugs resistance results. Statistically differences ($P<0.05$) were considered significant.

Results and Discussion

Out of 131 patients, the isolates from 113 (86.3%) patients were fully susceptible to all drugs (first line drugs) while 18 (13.7%) patients were resisted to one drug as mono-resistance or more drugs as multi resistance. The resistance to Isoniazid alone or in combination with other drugs was shown in 16 (12.2%) patients; figure (1). The response to Isoniazid drug is important because the drug effect on several genes that associated with mycolic acid biosynthesis in the TB bacterium .This rate was higher when compare with other studies, (Merzaa *et al*., 2011) has reported 1(2.6%) as Isoniazid monoresistan rate among new cases in northern provinces of Iraq (Dohuk, Kurdistan).

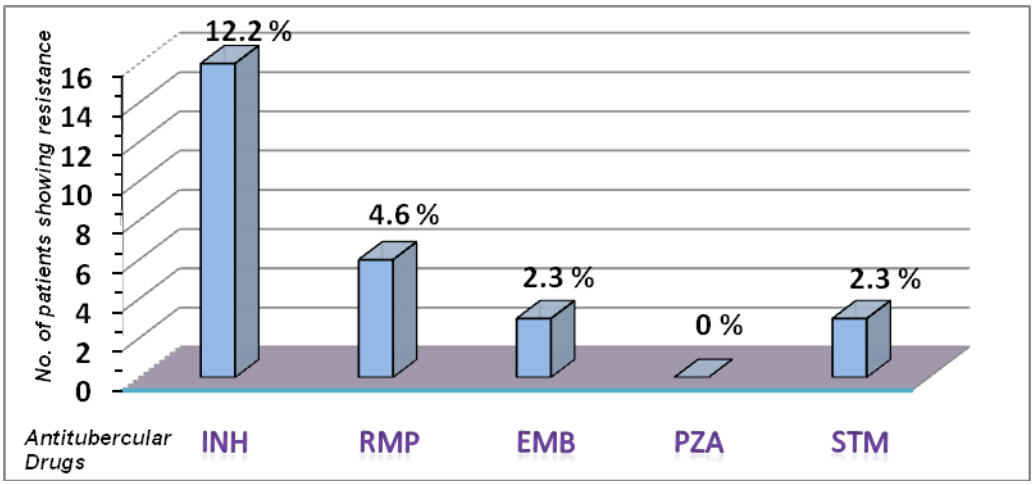

Figure (1): Monoresistance pattern of drug to present isolates.

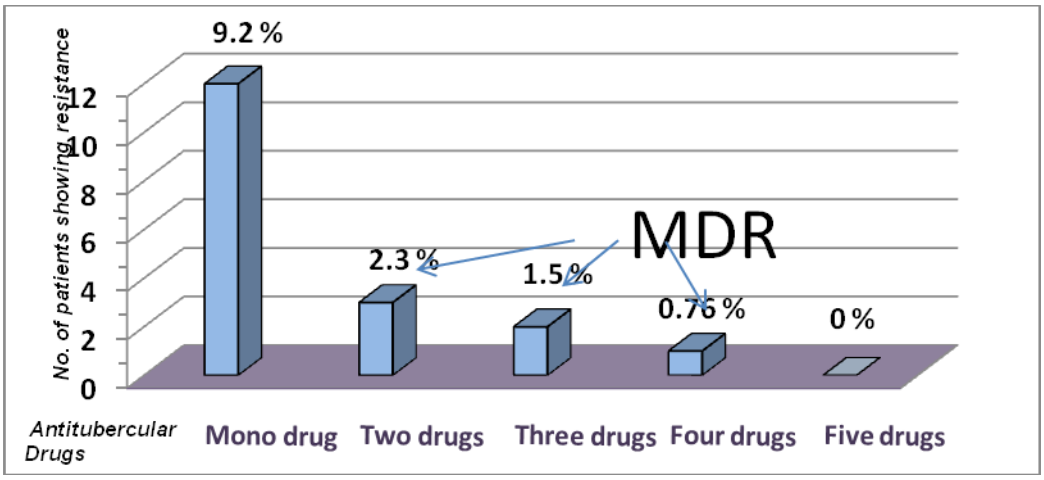

Figure (2): Multi resistance of drugs to present isolates.

followed by Rifampicin resistance in 6 (4.58%) patients and Although Rifampicin antibiotic having broader but never given as a single agent in the treatment of active tuberculosis because resistant strains rapidly emerge during therapy, therefore any defect in uptake of treatment , it will be emerge of multi drugs resistance and another explanation of our relatively high rate of Rifampicin resistance is attributed to its use in the treatment of non-specific infections as well as for certain infectious diseases like brucellosis (Richard *et al.*, 2006) . Further, the study found that all Rifampicin resistant strains also were resistant to Isoniazid. This is a common condition and has been reported by (Al-Orainey *et al.*, 1989). In such situations, treatment with INH and RMP will select strains resistant to both antimicrobials (WHO, 1997). It is well known that mono-resistance to Rifampicin is rare, whereas mono resistance to Isoniazid is common (Vareldzis *et al.*, 1994). Thus, the proposition to apply this fact in our TB laboratories, since there are limited resources for detecting MDR-TB strains in Iraq and no previously data dealing with this subject. And also Streptomycin resistant isolates 3 (2.3%) and the Ethambitul 3 (2.3%) was less common in this study since the widely used Ethambutal as a fourth drug in

the WHO standard regimen for new cases (Singh *et al.*, 2007). and No isolates were resisted to Pyrazinamide. The mono-resistance to Rifampicin, Ethambutal and Pyrazinamide not noted in present study and this confirmed with, (Merzaa *et al*., 2011) and in contrast with (Nema *et al.,* 2009). The present study has found that the rate of mono-resistance was 9.2 % and also the rate of multidrug resistance (MDR) with 6(4.6%) for new cases; figure (2), compare with a high prevalence rate of MDR-TB was seen in Saudi Arabia (6.8%) that reported by (Al-Tawfiq *et al.*, 2005) and Dohuk, Kurdistan with (7.9%) (Merzaa *et al*., 2011). In contrast to reports of WHO Iraq that estimated the percentage of Multi-Drug Resistance TB among new cases in Iraq is 3%, and among retreatment cases it is 38% (WHO Iraq, 2010).

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التحري عن فعالية الادوية المقاومة للسل في مستشفيات محافظة المثنى

الخلاصة

اجريت هذه الدراسة لبيان فعالية الادوية المضادة للسل بين حالات الجديدة من الاصابة, اظهرت النتائج ان 18 عزلة مقاومة لادوية الخط الاول من العلاج المضاد للسل first line anti-tubercular treatment Isoniazid, Rifampicin, Ethambutol, Streptomycin and Pyrazinamide)) مع مختلف انماط المقاومة من بين 131 عزلة حيث وجدت المقاومة المنفردة للدواء Mono-resistance في 12 (9.2%) عزلة, والمقاومة لاثنين من الادوية في 3 (2.3 %) عزلة والمقاومة لثلاثة من الادوية في 2 (1.5%) عزلة والمقاومة لاربعة من الادوية في 1 (0.76%) عزلة , في حين وجدت مقاومة لل MDR في6 (4.6%) من المرضى.